WHAT FACTS OF DIAGNOSTIC OR PROGNOSTIC VALUE CAN BE DETERMINED FROM TEST-MEAL EXAMINATION OF PATIENTS WITH GASTRIC SYMPTOMS?

A CLINICAL ANALYSIS OF 7041 CONSECUTIVE CASES EXAMINED BY A UNIFORM METHOD.[1]

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The work forming the basis of this report was personally performed in my services at the Mayo Clinic and at Augustana Hospital. A close association of clinical, laboratory, and operative observations was possible in 7041 consecutive patients. Independent records were kept of histories, analytical data, and pathological findings. When the individual case had been finally disposed of the facts determined independently were grouped. In this way, unbiased, non-subjective information was assured.

The patients of this series came on account of self-styled "dyspepsia" or "indigestion," or, in the routine history taking, symptoms were elicited which pointed to some primary or secondary gastric disturbance. Their ages ranged from fifteen to seventy-eight years; there were two males to each female; while all occupations were represented, yet it is interesting to note that 32 per cent. of the patients were from farms or rural communities. The average length of time of the period of gastric disturbance was 6.4 years. The shortest time was two weeks (a case of inoperable cancer) and the longest period was more than forty years.

Methods. The emptying power of the stomach was estimated by the administration of a physiological meal of mixed food after the patient had been taken off "diet" and his stomach was, as far as possible empty. Experience taught us that a twelve-hour time interval was of greater diagnostic worth than the four- to six-hour interval as recommended by Riegel and others. The secretory factor was determined by means of the Ewald breakfast of second day bread. This was selected on account of its ease of administration, its lack of disagreeable features, its constancy, and its facility of removal. In the ordinary case the time limit was fifty minutes after administration. Where clinical symptomatology indicated abnormally rapid emptying power the stomach was examined from twenty-five to forty minutes after the test-meal had been given. The size and position of the stomach were determined by inflation through the stomach tube, with the patient recumbent. We used an inflation bulb, expelling one and a half ounces of air at each compression. The boundaries of the stomach were determined by the auscultatory method while the inflation was in progress.

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In the space allotted for this paper only a brief summary of the work can be attempted. A detailed report is in preparation. It is difficult to present the work without its being merely statistical. A attempt has, however, been made to emphasize the clinical pointings.

SIZE OF STOMACH. The average capacity of the stomach was twenty-seven ounces in females and thirty-three ounces in males where dilatation did not exist. In instances revealing dilatation the average capacity in females was forty-one ounces and fifty-two ounces in males. The greatest gastric capacity was associated with non-malignant, pyloric stenosis.

THE MACROSCOPIC APPEARANCE OF REMOVED GASTRIC EXTRACTS. In addition to evidences of gastric retention this observation was not infrequently of significance.

Color. Traumatic blood was noted in 6.4 per cent. of all cases. Its presence was quite as constant when simple spasm existed at the cardia as when ulceration was present with or without spasm. Its appearance upon lavage had *no consistent relation to any form of gastric disease other than cancer.* Forty-four cases of gastric ulcer had lavage less than forty-eight hours following hemorrhage, and in these cases there was no recurrence of either gross or microscopic bleeding from the maneuver. In the cancer cases (96 per cent. being of the medullary type) traumatic blood on lavage was observed in more than half of the 218 consecutive cases.

Bile Coloring. Various shades of green or yellow were observed in 11 per cent. of the cases in the series. The yellowish shades were the results of straining as a consequence of tubing or occurred in 74 per cent. of the patients who had had a previous gastroenterostomy (seventy-six). The green coloration from bile was noted quite constantly in cases of gastric atony, ptosis with relaxed pylorus, dilatation with or without ptosis, intermittent pyloric spasm, induration about the pylorus due to ulcer or cancer, and from obstruction below the papilla of Vater. The green shades usually indicated that bile had been present in the stomach for some hours and had become oxidized. In two instances the growth of a chlorophylaceous mould was mistaken for bile before chemical tests or microscopic examination had been made. In 196 instances the presence of much traumatic blood rapidly hid evidences of bile coloring.

Of the cancer cases it is interesting to observe that coffee-colored or dark-brown extracts were noted in but 19 per cent. When such were observed the cases were inoperable. The color of gastric contents was quite as apt to be tan or brownish in partial stenosis with dilatation or atony from non-malignant causes as from cancer.

As will be shown below, however, the odor was a fairly reliable differentiating point between the two conditions. There were 314 cases of achylia gastrica. In 96 per cent. of this group the *dead-white* color of the gastric extract, associated with markedly absent chymification, was a characteristic finding.

Odor. Extracts from normal stomachs have a peculiarly, bland and somewhat sweetish odor. Modifications—quantitative and qualitative—in acidity cause variations. In non-retention cases the sharpness of the sour odor is usually a reliable gauge of the free hydrochloric acid content. In retention cases, high or low free hydrochloric acidity may be masked by the odor from fermentative or putrefactive processes. In 84 per cent. of the cancer group of this series, acrid, rancid odors due to volatile, organic acids were almost pathognómonic. In 76 per cent. of the non-malignant retention class (ulcers, gall-bladder disease, or ptosis with or without atony) the yeasty aroma was almost similarly characteristic. This simply elicited sign proved in our experience to be extremely useful in differential diagnosis. Putrefactive odors are generally due to sloughing of cancer tissue, deterioration of a quantity of blood in the presence of low hydrochloric acidity, fecal contents from obstruction below the duodenum or from perforation of ulcer or cancer into an adjacent viscus.

Amount of Gastric Extract. The average quantity of test-meal removed in the entire series was 108 c.c. The average quantity in the non-retention group was 76 c.c. The average quantity in the retention class was 350 c.c. So-called "hypersecretion" was as frequently observed in pyloric spasm from appendix or gall-bladder disease as from duodenal or gastric ulcer. It is not difficult to mistake partial pyloric stenosis for irritive hypersecretion. But 21 per cent. of the non-stenosing ulcers (duodenal or gastric) exhibited what might be termed hypersecretion. In young adults of both sexes the most common association of hypersecretion was pyloric spasm with diseased appendix or gall-bladder. Some degree of such was constantly present if the symptoms had persisted longer than an average time of 2.8 years.

Mucus. Mucus is a sign of doubtful diagnostic worth. It is more commonly in excess in stenosing cancers or ulcers than when the pyloric channel is free. While 1 per cent. of hyperacidity and hypersecretion cases were associated with pathological increase in mucus, 46 per cent. of the malignant retention group and 29 per cent. of the non-malignant retention class revealed such increase.

Chymification is an index of masticatory thoroughness, of the character of food ingested, of the combining power of hydrochloric acid, of the presence of normal gastric ferments, and of variations in gastric peristalsis and empyting power. The last factor appears to carry the greatest weight in all cases except those of primary or secondary achylia While high hydrochloric acid content generally assures good chymification, the presence of organic acids and foreign microörganisms (as in gastric cancer) frequently accomplishes similar ends.

The Incidence of Retarded Gastric Emptying Power. This term "emptying power," is especially chosen. "Hypermotility" should be largely limited to what is indicated by "hyperperistalsis." It does not necessarily follow that hyperperistalsis is associated with increased or even normal rate of the stomach's emptying. In fact, our records demonstrate that hyperperistalsis is most commonly found in instances of pyloric spasm or pyloric stenosis that have gastric or extragastric foundation.

Of our entire series, 12 per cent. of the cases showed some grade of retarded gastric emptying power macroscopically. In 8 per cent. of the series this was a *constant* finding. In 4 per cent. it was an intermittant manifestation. In 87 per cent. of the group when gastric retention was a persistant observation, some degree of gastric dilatation was an associated complication. In two out of every three cases where this occurred there was clinical history of delayed vomiting. Some of our most marked instances of gastric dilatation proved to have almost perfect emptying power. Persistent demonstration of gastric retention is an indication for surgical intervention. It denotes mechanical abnormalities or obstruction. In these instances, dilatation of the stomach is a symptom and not the disease. In a given case the degree of gastric retention may vary markedly accordingly as the stenosis is or is not associated with gastric or pyloric spasm. Dilatation of the stomach may likewise vary greatly in degree.

In our series the causes of persistent gastric retention were, in the order of the frequency of their demonstration, gastric cancer, duodenal ulcer, gastric ulcer, cholecystitis with adhesions, gastric atony, tumor of the pancreas, tumor of the liver, hypernephroma, tuberculous peritonitis, and retroperitoneal sarcoma. The causes of intermittent gastric retention were pyloric spasm associated with appendicitis or cholecystitis, gall-stones, duodenitis or gastritis in the presence of increased free hydrochloric acid, and gastroptosis.

In gastric cancer, emptying power was retarded in more than 70 per cent. of instances, irrespective of the location of the growth. In surgical duodenal ulcer, approximately two out of three cases revealed gastric stagnation. In surgical gastric ulcer in rather more than 50 per cent. of instances some grade of retention was proved. Of the pyloric spasms, associated with appendicitis, cholecystitis, gall-stones, or duodenitis, in rather more than 3 per cent. of instances retention was demonstrated. The sign of differential worth in this class of case is that of the variability of the exhibition of retention at different examinations. This sign is of special value to the surgeon who contemplates gastro-enterostomy in such instances. Unless definite obstruction exists at or near the pylorus the best operative results are only to be expected when artificial stricture is surgically produced. We have the records of the examination of 482 cases of pyloric spasm with intermittent gastric retention, when later the appendix had been removed or operations upon the gall-tract had been performed. In but twenty-one instances was any form of gastric stagnation subsequently demonstrated.

These observations of the incidence of gastric retention, cannot in any way be compared with such information returned from examination by means of the Roentgen ray. It should be urged that, in the method outlined, we are dealing with physiological problems as they occur in a given individual. No one has yet shown that the examinations of gastric function by means of bismuth or barium compounds with the aid of the Roentgen ray is physiological. Consequently, only a long series of observations that have been checked up by surgical procedure or by the subsequent history in medical cases, extending over several years' time, will enable actinologists to formulate statements that will indicate what meaning we can attribute to retention of bismuth or barium in the stomach at the end of, say, a six-hour interval.

The most common causes of increased rate of emptying of the stomach in our series occurred in conjunction with achylia gastrica (primary or associated with severe anemia), vagus hypotonia, temporary or permanent atony without marked gastric dilatation, non-obstructing gastric cancer, colitis, and in numerous nervous states of the young adult.

Gastric Acidity. During the past five years, attempts have been made to belittle the significance of estimations of gastric acidity. This attitude has been brought about largely because of the persistence of surgical teachings. It is expected that those who anticipated that a simple color test would serve in place of clinical cerebration would be doomed to disappointment. While we have been compelled to revise some of our previously held opinions regarding the diagnostic worth of acid estimations of gastric extracts, yet when considered as a part of evidence making for proper conception of disease it would seem that such information can in no wise be neglected. The confusion has arisen chiefly because it was not until recently shown, just what effect upon gastric physiology had extragastric disease. Consequently, the findings in disease extrinsic to the stomach were interpreted, clinically, in the light of known primary gastric ailments.

For the purpose of brevity we would classify our acidity findings under three groups; (1) that comprising recognized disease of the stomach itself; (2) that including lesions of the duodenum, gall-bladder, appendix, and the large bowel; (3) that comprising so-called functional or central disturbances.

Acidities were all estimated by the Toepfer method.

GROUP 1.—ACIDITY IN INTRINSIC GASTRIC DISEASE.

(*a*) Acute gastritis:	
Average—Free HCl	32.0
Total acidity	50.0
Combined acidity	18.0
(*b*) Chronic gastritis:	
Average—Free HCl	42.0
Total acidity	62.0
Combined acidity	14.0
(*c*) Chronic atrophic gastritis:	
Average—Free HCl	12.0
Total acidity	21.0
Combined acidity	9.0
(*d*) Achylia gastrica:	
Average—No free HCl	
Total acidity	8.0
Combined acidity	6.0
(*e*) Gastric ulcer—acute:	
Average—Free HCl	64.0
Total acidity	78.0
Combined acidity	12.0
(*f*) Gastric ulcer with recent hemorrhage:	
Average—Free HCl	35.0
Total acidity	48.0
Combined acidity	13.0
(*g*) Chronic non-retention gastric ulcer:	
Average—Free HCl	42.5
Total acidity	55.0
Combined acidity	13.5
(*h*) Chronic gastric ulcer with retention:	
Average—Free HCl	56.4
Total acidity	74.2
Combined acidity	17.8
(*i*) Chronic perforating ulcer:	
Average—Free HCl	64.1
Total acidity	76.2
Combined acidity	12.0
(*j*) Ulcus carcinomatosum—(64 cases):	
Average—Free HCl	33.4
Total acidity	51.0
Combined acidity	16.0
(*k*) Primary gastric cancer—(122 cases):	
Average—Free HCl	7.46
Total acidity	28.3
Combined acidity	21.0
(*l*) Ulcerating primary gastric cancer (14 cases):	
Average—Free HCl	2.0
Total acidity	34.0
Combined acidity	30.0

SUMMARY. *Group* 1. It is shown that the highest gastric acidities are uniformally determined in acute and subacute perforating ulcer of the stomach; that in simple, chronic gastritis the picture from the stand-point of acidity closely resembles that of ulcus carcinomatosum or of simple gastric ulcer when recent bleeding has occurred, that only 54 per cent. of cases of gastric cancer reveal absent free hydrochloric acid; that in 45 per cent. of instances of gastric cancer the acidity returns may be readily confused with those of simple gastric ulcer, chronic gastritis, or achylia gastrica unless the figures are rigidly interpreted in the light of clinical history, etc.; that in gastric ulcer with retention there is an increase in both free hydrochloric and total acidity, which fact is in sharp contrast to instances of retention developing in gastric cancer, in which event, as retention comes on, free hydrochloric is progressively lowered, while total acidity simultaneously increases. Other things being equal, in a given case, the diminution of free hydrochloric associated with an increase in total acidity, with the development of obstruction and the demonstration of organic acids, speaks for malignancy.

GROUP 2.—ACIDITY WHERE THE LESIONS ARE MAINLY OUTSIDE THE STOMACH.

(*a*) Duodenitis with pyloric spasm:	
Average—Free HCl	68.0
Total acidity	74.0
Combined acidity	6.0
(*b*) Duodenal ulcer without stenosis:	
Average—Free HCl	59.2
Total acidity	73.0
Combined acidity	14.0
(*c*) Duodenal ulcer with stenosis:	
Average—Free HCl	46.0
Total acidity	84.0
Combined acidity	28.0
(*d*) Cholecystitis, subacute:	
Average—Free HCl	66.0
Total acidity	71.0
Combined acidity	5.0
(*e*) Cholecystitis, chronic:	
Average—Free HCl	32.0
Total acidity	46.0
Combined acidity	14.0
(*f*) Appendicitis, subacute or chronic (usually in young adults both sexes):	
Average—Free HCl	64.0
Total acidity	75.0
Combined acidity	8.0
(*g*) Colitis, subacute or chronic:	
Average—Free HCl	35.0
Total acidity	42.0
Combined acidity	7.0
(*h*) Following gastro-enterostomy for gastric or duodenal ulcer:	
Average reduction in free hydrochlic acid	17.0
Total acidity	32.0
Combined acidity	12.0

SUMMARY. *Group* 2. Of this division the highest free hydrochloric acidities are present in cases of pyloric spasm associated with subacute cholecystitis, appendicitis, and duodenitis. The figures closely resemble those returned in gastric ulcer, as does also the clinical history with the exception of the incidence hemorrhage or chemical proof of bleeding and the time factor. The onset of stenosis in duodenal ulcer increases combined acidity at the expense of the free hydrochloric acidity. After gastro-enterostomy for non-malignant stenosis there is a consistent and noticeable lowering of free hydrochloric and also total acidity, which cannot, apparently, be wholly explained on the basis of regurgitation of *succus entericus*. In more than three out of four such instances, proof of this having occurred, can, however, be demonstrated by ferment tests or microscopic examination of stained smears.

Group 3.—Functional and Central Disturbances.

(*a*) In epilepsy of the young adult:	
Average—Free HCl	56.0
Total acidity	62.0
Combined acidity	5.0
(*b*) In neurasthenia, with or without moderate gastroptosis:	
Average—Free HCl	34.0
Total acidity	46.0
Combined acidity	9.0
(*c*) In marked gastroptosis:	
Average—Free HCl	37.0
Total acidity	52.0
Combined acidity	14.0

These figures interpret themselves and require no special comment.

The demonstration of altered or occult blood in gastric extracts by the benzidin or the guaiac tests was possible in 25 per cent. of the cases in the entire series. It was present in 42 per cent. of all retention cases irrespective of the causative lesion. It was demonstrated in 75 per cent. of the 712 cases of gastric cancer. It was almost as frequently shown in duodenal as in gastric ulcer. It would seem that apart from the association of occult blood with malignant processes, its demonstration in gastric extracts has very slight clinical worth.

The Incidence and Significance of Organic Acids in Gastric Extracts. These are rarely demonstrated in non-retention cases, either malignant or non-malignant. In malignant disease, associated with partial stenosis and gastric dilatation, lactic acid was present in 53 per cent. of 712 operatively demonstrated instances. It was rarely demonstrated when free hydrochloric acid rose as high as 10, and in 92 per cent. of cases where lactic acid was found, extensive growths, generally inoperable, were present. Only 3 per cent. of the non-malignant achylias were associated with lactic acid. In but 7 per cent. of the non-malignant retention cases was lactic acid present. It was found in less than 0.5 per cent. of instances of ptosis with atony.

Volatile fatty acids were present in 61 per cent. of the malignant cases and in but 3.2 per cent. of the instances of benign retention or atony. In no instance of non-retention or of simple achylia or hypoacidity were volatile fatty acids demonstrated.

The Significance of the Demonstration of Specific Ferments in Gastric Contents. Space does not permit our going into detail respecting the incidence and diagnostic worth of proving the absence or presence of pepsin and rennin in gastric extracts. It would seem that proteolysis is closely associated with the presence of free hydrochloric acid, so long as the acid concentration is below 0.4 per cent. and that milk-curdling ferment follows similar laws. In malignancy peptolysis appears to be increased at the expense of proteolysis.

We have made observations upon 827 instances of gastric disease for the detection of specific ereptases in gastric juices,[2] in the hope of recognizing early gastric cancer or malignant ulcer. We have used the *formaldehyde* titration method as suggested by Sorenson and Schiff. In our experience the average formol titration index in 87 instances of proved gastric cancer was 22.3; the average index in 22 cases of ulcus carcinomatosum was 19.8; the average in 99 cases of duodenal ulcer was 12.4; of 57 cases of simple gastric ulcer 11.6; of 32 cases of benign achylia, 14.1; of 16 instances of pernicious anemia, 14.5; and of 5 cases of cancer of the liver, 4.25. It would appear that in certain instances the estimation of the ereptic power of gastric juice toward peptone solutions is of considerable value when interpreted in the light of clinical history and symptomatology.

We have examined 108 cases for proteolytic ferments by the edestin method, suggested by Fuld and Levison.[3] The results thus far would appear to indicate that early cases of cancer of the stomach, where the free hydrochloric acid is shown to be low show high peptolysis and low proteolysis. In the simple ulcers both peptolysis and proteolysis are low.

We have already mentioned elsewhere our expereince with the demonstration of peptid-splitting ferments in gastric juice, using solutions of glycyltryptophan as the test dipeptid.[4] We made more than 1600 observations. In rather more than 40 per cent. of our proved cases of cancer (186) the reaction was positive. In about 7 per cent. the tryptophan test was positive. Diagnosis of malignant disease of the stomach was in each case quite possible, independent of the chemical test. While gastric abnormalities other than cancer exhibited positive glycyltryptophan reactions, in no class of the disease of the stomach was the test so frequently obtained as in cancer. Low free hydrochloric acid was frequently associated with positive glycyltryptophan tests, and in more than 50 per cent. of these reactions the gastric extracts contained bile or blood or both.

Wolff-Junghans' Test for Soluble Albumin in Gastric Extracts. We have tested 747 gastric extracts where there was low or absent free hydrochloric acid, quantitatively for soluble albumin,[5] according to the method suggested by Wolff of Ewald's clinic. Our work appears to indicate that in cancer this test was a more constant finding than when estimations for presence or absence of hydrochloric acid, of lactic or fatty acids, or of positive glycyltryptophan tests. It was approximately as constant a finding as tests for altered blood and the demonstration of motor inefficiency. It was not so constantly positive as the demonstration of organisms of the Boas-Oppler type or increase in the formol index. In extragastric malignancy and in gastric syphilis the manifestations of the test were inconstant. In the differentiation between malignant and non-malignant achylias the Wolff test, when interpreted in connection with other clinical and laboratory data, proved of considerable value. Positive manifestations were rarely obtained in the achylias of pernicious anemia, simple achylia gastrica and simple achlorhydrias not associated with gastric retention. Simple gastric and duodenal ulcers when accompanied by pyloric stenosis or marked gastric dilatation give confusing responses to the Wolff technique.

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[2] To be reported shortly.
[3] Biochem. Zeitsch., Bd. vi, Heft 5 u. 6, S. 473.
[4] Smithies, Arch. Int. Med., September, 1912, p. 672.
[5] Smithies, Amer. Jour. Med. Sci., May, 1914, p. 713

Significance of the Microscopic Examination of Gastric Extracts. We have made 6283 microscopic examinations (using the high power) of unfiltered gastric extracts that have been stained by the agar differential staining technique which we devised about three years ago.[6] In brief the summary of our work is as follows:

Starch digestion is not a constant index of the acidity of the stomach juice. Diastatic action of saliva often depends more on motor conditions than upon secretory. The character of the ingested food is a modifying factor. In some instances of low gastric acidity, with normal motility, it would seem that an anti-diastase were present in gastric extracts.

Microscopic remnants of the motor meal have no diagnostic significance other than that indicated when found in association with food macroscopically.

The Diagnostic Significance of the Microörganisms in Gastric Extracts. From our studies we have developed four microscopic pictures which seem almost pathognomonic for certain types of disease. Apart from these we can see nothing very significant. Certainly high gastric acidity by no means insures bacteriologic cleanliness.

Complex 1. *That of benign gastric retention* (*usually ulcer*). In 89 per cent. of our cases of this type the presence of large numbers of actively budding yeasts, associated with large and small sarcinæ and bacilli, apparently of the colon group, and food bits were demonstrated. The gastric acidity was generally above 50.

Complex 2. *That of gastric cancer.* In 93.8 per cent. of all our proved, late, malignant cases, organisms of the Boas-Oppler group, associated with food retention and acid averaging below 10, was a characteristic picture. In but 30 per cent. of instances were budding yeasts concomitant. In but 10 per cent. were sarcinæ associated. Threads of streptococci were found in 6.2 per cent. (more commonly in the non-retention group). There is no characteristic microscopic picture of early gastric cancer other than that associated with gastric ulcer of the retention type. In less than 1 per cent. of our cases of gastric cancer were we able to demonstrate so-called "cancer cells" with active mitoses. These were all late cases or cases where the cardiac orifice was involved with a sloughing growth.

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[6] Smithies, Arch. Int. Med., June, 1912, p. 736.

Complex 3. *Achylia Gastrica. Primary or Secondary.* In gastric extracts of low or absent hydrochloric acid, when there is atrophy of the mucosa and where motility is not interfered with, there are found long chains of streptococci (resembling beads of a rosary); groups of large, deep-staining cocci, and a peculiar, short, fat, acid-fast rod or cocco-bacillus that grows in short chains or pairs, or alone.

Complex 4. When perforation into an adjacent viscus has taken place in malignant ulcer or primary cancer, or where obstruction has occurred below the duodenum, the picture of immense numbers of thick cocco-bacilli, with or without spirillæ or streptococci, in association with low acidity, retarded food progress and putrefaction, as evidenced by the odor, is shown in more than 94 per cent. of instances.

THE PRESENCE OF CONTINUED HIGH TEMPERATURE IN MALIGNANT TUMORS.

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The presence of continued high fever in malignant tumors is a symptom that has not been sufficiently emphasized by the majority of clinicians. That it does occur in a considerable number of such cases is undoubtedly true, as the study of large series of cases by various authors shows. The purpose of the writer is to report a typical example of continued high temperature in adenocarcinoma of the kidney, with a review of the literature.

The case I wish to report was that of a man, aged forty-four years, who was admitted to Lakeside Hospital, April 19, 1911, complaining of pain in the left side of the abdomen during the preceding four months. The family history was of no importance, except that one sister had died of cancer, and another sister had been operated on several years ago for a fibroid tumor of the uterus which had undergone sarcomatous degeneration. There had been